IN THE SPECIFICATION:

Please REWRITE the paragraph at page 5, lines 12-19, as follows:

In another aspect, the present invention is directed to an isolated nucleic acid sequence, comprising (i) a first nucleic acid sequence segment encoding 1 to 15 amino acid residue N-terminal peptide fragment (S-peptide) of bovine or human ribonuclease A (the human homolog of bovine ribonuclease A is also known as ribonuclease I as described in Raines, R.T., Ribonuclease A 98:1045-1065 (1998)), and (ii) a second nucleic acid sequence segment encoding any full-length or mutated isoform of human vascular endothelial growth factor (VEGF), wherein the isolated nucleic acid sequence codes for a fusion protein which specifically binds adapter protein recognized by the polypeptide encoded by the first nucleic acid, and specifically binds to receptors for vascular endothelial growth factor recognized by the polypeptide encoded by the second nucleic acid sequence.

B1

Please REWRITE the paragraph at page 13, lines 8-23, as follows:

As used herein interchangeably, "S-peptide fragment of ribonuclease", "S-peptide", or "S-tag" refers to a 15 amino acid fragment of bovine pancreatic ribonuclease A with the following amino acid sequence: Lys-Glu-Thr-Ala-Ala-Ala-Lys-Phe-Glu-Arg-

B2

Gln-His-Met-Asp-Ser (SEQ ID NO:1), or to a 15 amino acid fragment of human ribonuclease A (also known as ribonuclease I as indicated above) with the following amino acid sequence: Lys-Glu-Ser-Arg-Ala-Lys-Lys-Phe-Gln-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:2), that can associate with the S-protein fragment of ribonuclease A forming the associate known as ribonuclease S for bovine protein. It is understood that the S-peptide may be used as modified by amino acid substitutions, amino acid deletions, amino acid insertions, and amino acid additions, as in fusion protein that do not eliminate the ability of the peptide to bind to S-protein fragment of ribonuclease. Such operational definition of S-peptide encompasses peptide fragments from ribonucleases of other species that may bind to appropriate protein fragment. Vectors for the expression of fusion proteins with bovine S-tag are commercially available. Vectors for the expression of fusion proteins with human S-tag are constructed using techniques known in the art by insertion of DNA sequence encoding the human S-tag with the composition Lys-Glu-Ser-Arg-Ala-Lys-Lys-Phe-Gln-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:2) in the commercially available expression vectors.

Please REWRITE the paragraph at page 29, lines 7-9, as follows:

The primers corresponding to the "sense" strand of human ribonuclease A cDNA (SEQ ID NOS:14, 15, and 16) included AUG codon immediately upstream of the DNA codon for amino acid 16,

B3 Cont'd

19, and 21 of the human ribonuclease A (also known as ribonuclease I), respectively.

Please REWRITE the paragraph at page 32, lines 13-23, as follows:

A single-stranded DNA fragment (SEQ ID NO:27) corresponding to the "sense" strand of human ribonuclease A (also known as ribonuclease I) cDNA encoding S-peptide Lys-Glu-Ser-Arg-Ala-Lys-Lys-Phe-Gln-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:28) and a complementary single-strand DNA fragment (SEQ ID NO:29) were mixed at equimolar concentrations and annealed at room temperature for 10 min. The fragments were designed to reconstitute 5'- Nde I site upstream of K1 codon and 3'-Kpn I site downstream of S15 codon after annealing. The annealed DNA fragment was ligated into a pET/VEGF121 vector between Nde I and the Kpn I sites. The resulted plasmid was designated pET/hus-VEGF121, and transformed into NovaBlue competent cells (Novagen, USA) according to the manufacturer's instructions. Bacterial cultures containing the desired plasmids were grown further in order to obtain large preparations of isolated plasmids using methods described in Example 1.A.2.

B4

Please REWRITE the paragraph beginning at page 33, line 27 and continuing to page 34, line 20, as follows:

To purify each of VEGF fusion proteins a corresponding cell culture pellet obtained as described in Example 1.C.1 was resuspended in ice cold buffer A (50 mM Tris-HCl pH 7,5, 0.1 mM $MgCl_2$, 0.1 mM DTT, 200 mg/L PMSF, 25 mg/L antitripsin, 50 mg/L leupeptin, 25 mg/L aprotinin). After five cycles of freezing and thawing DNAse was added to the cell suspension, 50 U per ml. The suspension was incubated for 20 min at room temperature; then centrifuged at 5,000xg for 30 min at 4°C. The inclusion bodies pellet was solubilized in 10 ml of 8 M urea, followed by sonication for 5-10 min in an ice-cold water sonicator (FC 14, Fisher Sci., USA) and the protein solution was clarified by centrifugation at 14,000xg for 10 min, at 4°C, and the supernatant was dialyzed against 10 mM Tris-HCl pH 8.0, 150 mM NaCl for 16 hours at 4°C. VEGF fusion proteins obtained as described here were 75-90% pure as judged by Coumassie-stained SDS-PAGE analysis. VEGF fusion proteins containing thioredoxin were designated txVEGF121, txVEGF165, and txVEGF189. VEGF fusion proteins without thioredoxin were designated FVEGF121, FVEGF165 and FVEGF189. The fusion protein consisting of 16-124 aa fragment of bovine ribonuclease A linked to human VEGF121 via 7 aa linker GTDDDDK (SEQ ID NO:30) was designated 16-BoS-VEGF121. The fusion protein consisting of 1-15 aa fragment of human ribonuclease A (also known as ribonuclease I) linked to human VEGF121 via 7 aa linker GTDDDDK was designated hus-VEGF. The concentrations of VEGF fusion protein with bovine S-tag were measured with a commercially available S-tag Rapid Assay Kit (Novagen, USA) based on quantitation of ribonuclease activity which is restored when a protein carrying the S-peptide fragment of ribonuclease (S-tag) is supplemented with the S-protein fragment of ribonuclease. Concentration of hus-VEGF was

If a telephone conference would aid in the continued prosecution of this application, the Examiner is invited and encouraged to contact Applicants' representative at the telephone number listed below.

Respectfully submitted,

MARINA V. BACKER ET AL.

By Todd E. Garabedian

Todd E. Garabedian, Ph.D.
Registration No. 39,197
Attorney for Applicants

WIGGIN & DANA
One Century Tower
New Haven, CT 06508
Telephone: (203) 498-4400
Fax: (203) 782-2889

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